General

Guideline Title

Taiwan osteoporosis practice guidelines.

Bibliographic Source(s)

Bureau of Health Promotion, Department of Health, Taiwan, National Health Research Institutes, Taiwanese Osteoporosis Association. Taiwan osteoporosis practice guidelines. Taiwan (ROC): Bureau of Health Promotion, Department of Health, Taiwan; 2011 Dec. 110 p. [261 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The grades of recommendations (A–D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Epidemiology of Osteoporosis

- Foreign reports showed that spine fracture is associated with a higher mortality rate. (Grade of Recommendation B, Level of Evidence 2++ [Cooper et al., 1993; Lips et al., 1999])
- National and foreign reports showed that hip fracture is associated with a higher mortality rate. (Grade of Recommendation B, Level of Evidence 2++ [Cooper et al., 1993; Chie et al., 2004])
- The information from the National Health Insurance (NHI) showed that hip fracture leads to higher mortality rate in both men and women. (Grade of Recommendation C, Level of Evidence 2++ [Chie et al., 2004])
- The correlation coefficient (r) of the results from dual energy X-ray absorptiometry (DXA) and quantitative ultrasound (QUS) is about 0.6. (Grade of Recommendation B, Level of Evidence 2+ [Njeh et al., 2000])
- The DXA results of all age groups in Taiwan are similar to those of Caucasians. (Grade of Recommendation C, Level of Evidence 2+ [Tsai et al., "Sexual differences," 1996; Tsai et al., 1991; Shen et al., 1994])
- 50% of middle-aged women in Taipei City have insufficient vitamin D intake. (Grade of Recommendation C, Level of Evidence 2+ [Tsai et al., 1997])
- The bone turnover markers of middle-aged and aged men and women show different senile changes, and a higher level of marker is related to lower bone density. (Grade of Recommendation C, Level of Evidence 2+ [Tsai et al., "Sexual differences," 1996])
- The risk of bone fracture is higher in individuals with longer femur necks. (Grade of Recommendation C, Level of Evidence 2+ [Yang,

Wang, & Liu, 1999])

- In Canada, the incidence of femur fracture decreased while the percentage of aged patient remained the same. (Grade of Recommendation B, Level of Evidence 2++ [Leslie et al., 2009])
- In 2010, about 15,000 aged individuals in Taiwan experienced hip fracture; the one-year mortality rate of men was 22%, and it was 15% for women. (Grade of Recommendation C, Level of Evidence 2++ [Chie et al., 2004], 2+ [Shao et al., 2009])
- In 1993, compression deformities of vertebral body were noted in 19.5% and 12% of women and men aged ≥65, respectively, in Taiwan. (Grade of Recommendation C, Level of Evidence 2+ [Tsai et al., "Prevalence of vertebral fractures," 1996])

Diagnosis of Osteoporosis and Follow-up

Assessments of Osteoporosis

Physical Examination (PE) and X-ray

- Osteoporosis Self-assessment Tool for Asians (OSTA) is a simple self-assessment tool for women. (Grade of Recommendation C, Level of Evidence 2+ [Koh et al., 2001])
- Low body weight (<51 kg) suggests the possibility of osteoporosis or spine fracture in Westerners, but the cutoff value is not yet available for Asians. (Grade of Recommendation C, Level of Evidence 2+ [Green et al., 2004])
- A teeth number of <20 is a predictor of osteoporosis or spine fracture. (Grade of Recommendation C, Level of Evidence 2+ [Green et al., 2004])
- The presence of hump is a predictor of osteoporosis and spine fracture. (Grade of Recommendation C, Level of Evidence 2+ [Green et al., 2004])
- A wall-occiput distance larger than 0 cm is a predictor of osteoporosis and spine fracture. (Grade of Recommendation C, Level of Evidence 2+ [Green et al., 2004])
- A rib-pelvis distance smaller than two fingerbreadths is a predictor of osteoporosis and spine fracture. (Grade of Recommendation C, Level of Evidence 2+ [Green et al., 2004])

Bone Turnover Markers

- Bone turnover markers assist in the assessment of bone formation and loss. (Grade of Recommendation C, Level of Evidence 2+ [Eastell & Hannon, 2008; Brown et al., "Bone turnover markers," 2009])
- Bone turnover markers are predictors of osteoporosis-related fracture. (Grade of Recommendation C, Level of Evidence 2+ [Eastell & Hannon, 2008; Brown et al., "Bone turnover markers," 2009])
- Bone turnover markers can be used to monitor the response to the treatment of osteoporosis. (Grade of Recommendation C, Level of Evidence 2+ [Eastell & Hannon, 2008; Brown et al., "Bone turnover markers," 2009])

Quantitative Ultrasound (QUS)

- Common cutoff points are unable to exclude or confirm the osteoporosis cases diagnosed by DXA. (Grade of Recommendation A, Level of Evidence 1+ [Nayak et al., 2006])
- Calcaneus QUS can be used to define the risk of osteoporosis-related bone fracture in postmenopausal women or aged men. (Grade of Recommendation C, Level of Evidence 2+ [Hans et al., 1996; Bauer et al., 1997; Bauer et al., 2007; Khaw et al., 2004])
- There is no difference between men and women when using calcaneus QUS for predicting the risk of hip fracture. (Grade of Recommendation C, Level of Evidence 2+ [Khaw et al., 2004; Fujiwara et al., 2005])

Dual Energy X-ray Absorptiometry (DXA)

- The diagnosis and evaluation based on the lowest T-score from the assessment of lumbar spine and hip bone using DXA is the gold standard in clinical practice. (Grade of Recommendation A, Level of Evidence 1+ [Lane, 2006; Blake & Fogelman, 2009] 1++ [Baim et al., 2008])
- When lumbar spine and hip bone are not available for DXA assessment, the non-dominant forearm can be used in the diagnosis and evaluation of osteoporosis. (Grade of Recommendation A, Level of Evidence 1+ [Lane, 2006; Blake & Fogelman, 2009] 1++ [Baim et al., 2008])
- The bone density in the lumbar spine, forearm and hip bone measured with DXA is a predictor of osteoporosis-related fracture. (Grade of Recommendation A, Level of Evidence 1+ [Lane, 2006; Blake & Fogelman, 2009] 1++ [Baim et al., 2008; Marshall, Johnell, & Wedel, 1996])
- DXA can be used for the follow-up of osteoporosis treatment, and the interval depends on the therapeutic intervention used. (Grade of Recommendation A, Level of Evidence 1+ [Lane, 2006; Blake & Fogelman, 2009] 1++ [Baim et al., 2008])

Diagnosis of Osteoporosis

Middle-aged or Aged Individuals (Men Aged ≥50 or Postmenopausal Women)

- The diagnosis of osteoporosis is suggested when the T-score of any axial bone (lumbar spine or bones in hip or non-dominant forearm) is up to -2.5. (Grade of Recommendation B, Level of Evidence 2++ [Kanis, 1994])
- The diagnosis of osteoporosis is suggested when a patient experienced, or had history of, low impact fracture of bones in hip or non-dominant forearm. (Grade of Recommendation B, Level of Evidence 2++ [Nelson et al., 2010; Lewiecki & Binkley, 2009] 4 [Blank et al., 2010)
- The diagnosis of osteoporosis is suggested when compression fracture is found in one or more vertebral bodies, and the patient does not have history of trauma or secondary conditions. (Grade of Recommendation C, Level of Evidence 2++ [Nelson et al., 2010] 2- [Genant et al., 1993])
- Quantitative ultrasound or other dual or single photon absorptiometry (peripheral bone densitometer) of other parts of body is better used for reference in screening and is not recommended to be used as a diagnostic tool. (Grade of Recommendation B, Level of Evidence 2++ [Kreig et al., 2008])
- Bone turnover marker cannot be used as a diagnostic tool. (Grade of Recommendation B, Level of Evidence 2++ [Baim et al., 2008])

Adults (Men Aged 20~49 or Premenopausal Women)

- The diagnosis of osteoporosis is suggested only when the patient has clinical low impact fracture, and the confirmed high risk of bone fracture as determined by the presence of low bone mass (or worse) indicated by the Z-score acquired from DXA. (Grade of Recommendation B, Level of Evidence 2++ [Baim, et al., 2008])

Indications for DXA Scan and Recommendations for Follow-up

Indications for Examinations

- Bone density testing using DXA should be performed on women aged ≥65. (Grade of Recommendation A, Level of Evidence 1++ [Nelson & Helfand, 2002; Nelson et al., 2002] 2++ [Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010)
- Bone density testing using DXA should be performed on postmenopausal women aged ≤65 with the risk factors of bone fracture. (Grade of Recommendation A, Level of Evidence 1++ [Nelson & Helfand, 2002; Nelson et al., 2002] 2++ [Hodgson et al., 2003; Baim, et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010])
- Bone density testing using DXA should be performed on men aged ≥70. (Grade of Recommendation B, Level of Evidence 2++ [Schuit et al., 2004; Van der Klift et al., 2002; Cummings et al., 2006; Gonnelli et al., 2005; Bauer et al., 2007; Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010])
- Bone density testing using DXA should be performed on men aged 50-70 with the risk factors of bone fracture. (Grade of Recommendation B, Level of Evidence 2++[Schuit et al., 2004; Van der Klift et al., 2002; Cummings et al., 2006; Gonnelli et al., 2005; Bauer et al., 2007; Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010])
- Bone density testing using DXA should be performed on individuals aged ≥50 with low impact fracture(s). (Grade of Recommendation B, Level of Evidence 2++ [Hodgson et al., 2003; Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010; Oyen et al., 2010])
- Bone density testing using DXA should be performed on individuals with conditions related to loss of bone mass. (Grade of Recommendation C, Level of Evidence 2++ [Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010]
- Bone density testing using DXA should be performed on individuals using medications related to loss of bone mass. (Grade of Recommendation B, Level of Evidence 2++ [Hodgson et al., 2003; Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010])

Follow-up

- Bone density should be monitored every 2 years for treated women aged ≥65. (Grade of Recommendation B, Level of Evidence 2++ [Baim et al., 2008; Dawson-Hughes et al., 2008; Nelson et al., 2010])
- Bone density should be monitored every 3 years for untreated postmenopausal women. (Grade of Recommendation D, Level of Evidence 2++ [Baim et al., 2008])

Clinical Risk Factor (CRF) and Fracture Risk Assessment Tool (FRAX)

Assessment of Clinical Risk Factors

- The One-Minute Osteoporosis Risk Awareness Test by the International Osteoporosis Foundation helps increase the number of individuals for screening, but this test cannot be used to identify osteoporosis. (Grade of Recommendation B, Level of Evidence 2++ [Baim et al.,

2008])

- The evaluation of clinical risk factors is unable to replace the role of bone densitometry in the diagnosis of osteoporosis. (Grade of Recommendation B, Level of Evidence 2++ [Baim et al., 2008; Oyen et al., 2010])

Fracture Risk Assessment Tool (FRAX)

- For Taiwanese aged 40-90, the Taiwanese FRAX formula can be used to obtain a quick glimpse of the risk of osteoporosis-related fracture. (Grade of Recommendation B, Level of Evidence 4 [Kanis et al., 2010; Kanis et al., 2008] 2++ [Shao et al., 2009])
- DXA and other examinations are recommended for untreated individuals whose ten-year overall risk of osteoporosis-related fracture is 10%~20%. (Grade of Recommendation D, Level of Evidence 4 [Kanis et al., 2010; Kanis et al., 2008])
- DXA and other examinations are recommended for untreated individuals whose ten-year risk of osteoporosis-related hip fracture is higher than 1.5~3%.(Grade of Recommendation D, Level of Evidence 4 [Kanis et al., 2010; Kanis et al., 2008])
- Intervention is recommended for untreated individuals whose ten-year overall risk of osteoporosis-related fracture is >20%. (Grade of Recommendation D, Level of Evidence 4 [Kanis et al., 2009])
- Intervention is recommended for untreated individuals whose ten-year risk of osteoporosis-related hip fracture is >3%. (Grade of Recommendation D, Level of Evidence 4 [Kanis et al., 2009])
- Economic and insurance factors should also be considered when determining the FRAX cut-offs for intervention. (Grade of Recommendation D Level of Evidence 4 [Kanis et al., 2009])
- FRAX is unable to replace the role of bone densitometry in the diagnosis of osteoporosis. (Grade of Recommendation B, Level of Evidence 2++ [Oyen et al., 2010)

Approaches for Prevention and Treatment of Osteoporosis without Medication

Diet

Calcium and Dairy Products

- Calcium intake is positively correlated to bone mineral accretion/bone density and decrease of bone mass loss. (Grade of Recommendation B, Level of Evidence 1- [Cumming, 1990; Welten et al., 1995] 2+ [van Beresteijn et al., 1990; Heaney, 2000] 2- [Riggs et al., 1987])
- Higher calcium dietary intake is associated with a lower risk of bone fracture. (Grade of Recommendation B, Level of Evidence 1- [Cumming, 1990; Welten et al., 1995] 2+ [Heaney, 2000])
- Dairy product intake is positively correlated to bone mineral deposit or bone mineral density (BMD). (Grade of Recommendation C, Level of Evidence 2+ [Heaney, 2000; Dietary Guidelines Advisory Committee, 2005; Heaney, 2009])
- Dairy product intake is not associated with the risk of bone fracture/is associated with a significantly lower risk of bone fracture (no related randomized controlled trials to date). (Grade of Recommendation C, Level of Evidence 2+ [Heaney, 2000])

Vitamin D

- Vitamin D deficiency is one of the main contributors of osteoporosis. (Grade of Recommendation B, Level of Evidence 1+ [Bischoff-Ferrari et al., "Prevention of nonvertebral fractures," 2009] 1- [Bischoff-Ferrari et al., 2005])
- The normal level of serum 25(OH)D (vitamin D status marker) is positively correlated to BMD. (Grade of Recommendation C, Level of Evidence 2++ [Bischoff-Ferrari, 2009])
- Vitamin D supplement has a dose-reaction relationship on the reduction in the risk of non-spinal and hip fractures and the level of serum 25(OH)D (when the serum level ≥75 nmol/L). (Grade of Recommendation B, Level of Evidence 1+ [Bischoff-Ferrari et al., "Prevention of nonvertebral fractures," 2009] 1- [Bischoff-Ferrari et al., 2005])
- Vitamin D can reduce risk of falls by improving muscle function. (Grade of Recommendation B, Level of Evidence 1+ [Bischoff-Ferrari et al., "Fall prevention," 2009]) 2++ [Bischoff-Ferrari, 2009])
- For individuals aged ≥65, the 25(OH)D levels are suggested to be kept at ≥75 nmol/L to effectively lower the risk of non-spinal fractures and falls. (Grade of Recommendation B, Level of Evidence 1+ [Bischoff-Ferrari et al., "Prevention of nonvertebral fractures," 2009; Bischoff-Ferrari et al., "Fall prevention," 2009] 2++ [Bischoff-Ferrari, 2009] 3 [Hanley et al., 2010])

Phosphorus

- Bone formation may be affected by phosphorus deficiency despite the concomitant administration of bone formation medication and high-dose calcium supplement. (Grade of Recommendation D, Level of Evidence 3 [Heaney, "Phosphorus nutrition," 2004])

Protein

- Protein intake is positively correlated to bone density, and the use of protein supplement is positively correlated to a higher bone density of lumbar spine. (Grade of Recommendation B, Level of Evidence 1+ [Darling et al., 2009] 2+ [Kerstetter, O'Brien, & Insogna, 2003])
- There is no significant correlation between the amount of protein intake and the incidence of hip fracture. (Grade of Recommendation B , Level of Evidence 1+ [Darling, et al., 2009] 2+ [Kerstetter, O'Brien, & Insogna, 2003])

Vitamin K

- Vitamin K supplement helps control the level of under carboxylated osteocalcin. (Grade of Recommendation B, Level of Evidence 2++ [Shea & Booth, 2008; Cashman & O'Connor, 2008])
- Low vitamin K1 (phylloquinone) intake (about 200-500 μg/d) has no significant effect on the bone density change of the lumbar spine and femoral neck. (Grade of Recommendation C, Level of Evidence 2++ [Shea & Booth, 2008; Cashman & O'Connor, 2008])
- Phylloquinone intake is associated with a lower risk of hip fractures. (Grade of Recommendation C, Level of Evidence 1- [Cockayne et al., 2006] 2+ [Iwamoto et al., 2009])
- The osteoporosis treatment using high dose (45 mg/d) of MK-4 (menaquinone-4, vitamin K2) provides protective effect for the bone density or bone fracture risk in the lumbar spine or palmar bone. (Grade of Recommendation C , Level of Evidence 1- [Cockayne et al., 2006] 2+ [Iwamoto et al., 2009])

Vegetarian

- The bone density in the lumbar spine and femoral neck of vegetarians is lower than that of non-vegetarians, and the difference in bone density is statistically significant between vegan and non-vegetarians; a less significant difference is found between lactoovovegetarians and non-vegetarians. (Grade of Recommendation C, Level of Evidence 1- [Ho-Pham, Nguyen, & Nguyen, 2009] 2++ [Smith, 2006])

Table Salt/Sodium

- Dietary salt/sodium intake is positively correlated with urinary calcium excretion. (Grade of Recommendation C, Level of Evidence 2+ [Teucher & Fairweather-Tait, 2003; Woo et al., 2009] 2- [de Wardener & MacGregor, 2002])
- Dietary sodium intake (as indicated by urinary sodium secretion) is negatively correlated with the bone density of hip bone and lumbar spine. (Grade of Recommendation C, Level of Evidence 2+ [Teucher & Fairweather-Tait, 2003; Woo et al., 2009])

Exercise and Activity

- Low to moderate intensity weight-bearing impact exercise - walking is associated with a consistent and significant improvement for the BMD in the femoral neck. Brisk walking provides better effect than casual walking, and the effect of longer intervention is longer than those of shorter periods. More significant effect is seen in individuals with lower BMD. (Grade of Recommendation A, Level of Evidence 1++ [Martyn-St James & Carroll, 2008] 1+ [Hatori, et al., 1993; Borer et al., 2007; Ebrahim et al., 1997; Yamazaki et al., 2004] 2++ [Feskanich, Willett, & Colditz, 2002] 1- [Palombaro, 2005])
- High intensity weight-bearing impact exercise - jogging and running improve the BMD in the lumbar spine, femoral neck and calcaneus. (Grade of Recommendation A, Level of Evidence 1+ [Snow-Harter et al., 1992; Williams et al., 1984] 2++ [Brahm et al., 1997; Suominen & Rahkila, 1991; Mussolino, Looker, & Orwoll, 2001])
- Mixed weight-bearing impact exercise - the combination of aerobic exercise including walking, jogging and stair climbing provides notable improvement in the BMD in several vital body parts (lumbar spine, femoral neck, proximal femur). (Grade of Recommendation A, Level of Evidence 1+ [Kohrt, Ehsani, & Birge, 1997; Heinonen et al., 1998; Kohrt et al., 1995; Dalsky et al., 1988; Heinonen et al., 1996])
- Special impact exercise - side stepping, jumping rope, stepping and stair stepping with a ground reaction force of ≥2x body weight improve the bone density in the lumbar spine and femoral neck in premenopausal and postmenopausal women. (Grade of Recommendation A, Level of Evidence 1+ [Heinonen et al., 1996; Grove & Londeree, 1992; Kato et al., 2006; Bassey & Ramsdale, 1994; Vainionpää et al., 2005; Vainionpää et al., 2009])
- Mixed resistive exercise/weight training provides notable improvement for the BMD in the lumbar spine and femoral neck, and the effect is site-specific. (Grade of Recommendation A, Level of Evidence 1++ [Martyn-St James & Carroll, 2006; Zehnacker & Bemis-Dougherty, 2007] 1+ [Wolff et al., 1999; Wallace & Cumming, 2000])
- Squash and tennis improve the BMD in the lumbar spine and limbs (that is, a site-specificity was noted), while long-term high-intensity training is required. (Grade of Recommendation B, Level of Evidence 2++ [Heinonen et al., 1995; Calbet et al., 1998])
- There is no medical evidence supporting the beneficial effect of swimming on the BMD, and long-term swimming training may lead to BMD loss in several body parts. (Grade of Recommendation B, Level of Evidence 1+ [Buie & Boyd, 2010] 2++ [Magkos et al., 2007; Morel et al., 2001])
- The medical evidence supporting the beneficial effect of cycling on the BMD is lacking, and long-term cycling training may lead to loss of BMD in lumbar spine. (Grade of Recommendation B, Level of Evidence 2++ [Nichols, Palmer, & Levy, 2003; Rector et al., 2008;

Smathers, Bemben, & Bemben, 2009; Penteado et al., 2010])
- The medical evidence supporting the effect of Tai Chi on controlling loss of BMD is inadequate. (Grade of Recommendation A, Level of Evidence 1++ [Li et al., 2011], 1+ [Lee et al., 2008; Rogers, Larkey, & Keller, 2009] 1- [Wayne et al., 2007])

Lifestyle

- A body mass index of ≤18.5 kg/m^2 is strongly discouraged. (Grade of Recommendation B, Level of Evidence 2++ [De Laet et al., 2005; Liu et al., 2008] 2+ [Wardlaw, 1996; Papaioannou et al., 2009] 4 [Pan et al., 2008])
- Avoid smoking. Smokers are encouraged to quit smoking to avoid the risk of osteoporosis and bone fracture. (Grade of Recommendation B, Level of Evidence 2++ [Law & Hackshaw, 1997; Ward & Klesges, 2001; Kanis et al., 2005; Wong, Christie, & Wark, 2007] 2+ [Hollenbach et al., 1993])
- Alcoholism is discouraged - control alcohol intake for better health. (Grade of Recommendation B, Level of Evidence 2++ [Turner, 2000] 2+ [Papaioannou et al., 2009])

Fall Prevention and Nursing Care

- No single assessment tool can be universally applied to every institution and/or different patients. Healthcare professionals must choose a fall assessment tool that is most appropriate for the patient based on the medical conditions. (Grade of Recommendation A, Level of Evidence 1+ [Scott et al., 2007])
- Patients with cataracts, glaucoma, or blurred vision should receive special treatment to correct visual acuity. (Grade of Recommendation A, Level of Evidence 1+ [Cumming et al., 2007; Harwood et al., 2005])
- Hip protectors can be provided to residents who live in skilled nursing homes, but the effect is limited in acute care. Wearing hip protectors may reduce hip fracture rate among nursing home residents. However, it did not show the same results at home or acute care settings (Grade of Recommendation A, Level of Evidence 1++ [Gillespie et al., 2009; Parker, Gillespie, & Gillespie, 2006; Oliver et al., 2007; Minns et al., 2004])
- Pharmacists review and provide a written summary of medications that may lead to falls. Review those medication side effects that could increase the risk of fall such as dizziness, and limb weakness. Educate the patients and caregivers accordingly. (Grade of Recommendation B, Level of Evidence 1++ [Zermansky et al., 2006])
- The use of multiple strategies of fall prevention in medical facilities is associated with lower risk of falling and falling-related injuries. (Grade of Recommendation B, Level of Evidence 1++ [Fonda et al., 2006; Oliver et al., 2008; Cameron et al., 2010])
- Primary care, community and acute care settings can use a multiple fall-prevention approach to prevent falls and related injuries. (Grade of Recommendation B, Level of Evidence 1++ [Gates et al., 2008])
- Heart disease should be treated (for example, pacemaker for arrhythmias). (Grade of Recommendation B, Level of Evidence 1++ [Gillespie et al., 2009])
- Healthcare professionals should be aware of the causes of previous falls, identify individuals at high risk for falls, and provide fall prevention warning signs to increase staff and caregiver's attention. (Grade of Recommendation D, Level of Evidence 4 [Centers for Disease Control and Prevention, 2008])
- Patients who take sedative/hypnotic agents should void the bladder before bedtime and avoid drinking water before going to bed. (Grade of Recommendation D, Level of Evidence 4 [Saskatoon Falls Prevention Consortium, 2009])
- Patients should wear low-heeled, comfortable, covered, non-slip shoes, and the right size clothes. Keep bathroom floors dry and install non-slip facility and hand rails. (Grade of Recommendation D, Level of Evidence 4 [Gray-Miceli & Capezuti, 2005])
- Place the aids, glasses, bed pans, or bedside nursing calls in a readily available place. (Grade of Recommendation D, Level of Evidence 4 [Centers for Disease Control and Prevention, 2008])
- Make sure that medications are reviewed and adjusted appropriately and gradually reduce sedative/hypnotics and anti-depression medications. (Grade of Recommendation D, Level of Evidence 4 [Saskatoon Falls Prevention Consortium, 2009])
- Increase the indoor lighting, allow an unobtrusive aisle at home and avoid protruding furniture. Electrical supplies wire should be attached to the wall. Daily supplies and appliances should be placed at the patient's waist level for easy access. (Grade of Recommendation D, Level of Evidence 4 [Centers for Disease Control and Prevention, 2008; Saskatoon Falls Prevention Consortium, 2009])

Surgical Management of Osteoporosis Related Problems

- Early surgical intervention, typically hip arthroplasty, should be provided to patients with hip fractures to facilitate early rehabilitation. (Grade of Recommendation A, Level of Evidence 1+ [Buchbinder et al., 2009])
- The rationale of early surgical intervention for spinal fracture patients without neural damage is inconclusive. (Grade of Recommendation B, Level of Evidence 1 [Kallmes et al., 2009])
- Vertebroplasty provides immediate pain relief to patients with acute spinal fractures. Please note that the patients should be told of the

potential risks of the treatment. (Grade of Recommendation C, Level of Evidence 3 [Wardlaw et al., 2009])
- Assistive device-based approach is effective in patients with non-weight-bearing limb fractures. (Grade of Recommendation C, Level of Evidence 3 [Chen et al., 2008])

Prevention and Treatment of Osteoporosis with Medication

Calcium

- Calcium supplement is associated with a lower risk of bone fracture in adults aged ≥50. (Grade of Recommendation C, Level of Evidence 2+ [Tang et al., 2007])
- Calcium supplement is associated with a lower risk of low traumatic fractures. (Grade of Recommendation D, Level of Evidence 2- [Bischoff-Ferrari et al., 2008])
- Calcium supplement alone may provide effective control over the risk of bone fractures in postmenopausal women. (Grade of Recommendation C, Level of Evidence 2++ [Flynn, 2004] 2- [Prince et al., 2006])
- Evidence regarding the beneficial effect of the concomitant use of calcium supplement and vitamin D on the risk of bone fracture remains controversial. (Grade of Recommendation D, Level of Evidence 2-)
- Calcium supplement (1000 mg) and vitamin D (400 IU/day) for healthy postmenopausal women provide little effect, and these may cause a higher risk of renal stones. (Grade of Recommendation C, Level of Evidence 2+ [Jackson et al., 2006])
- Calcium supplement alone, or in combination with vitamin D, is ineffective in the prevention of secondary bone fractures. (Grade of Recommendation B, Level of Evidence 1- [Grant, 2005])
- Calcium-fortified food is more effective in improving bone density than calcium supplement. (Grade of Recommendation D, Level of Evidence 3 [Manios et al., 2007])
- Concomitant use of calcium supplement and vitamin D delays bone loss in men aged ≥65. (Grade of Recommendation D, Level of Evidence 3)
- Calcium supplement provides little benefit to bone density of healthy children. (Grade of Recommendation D, Level of Evidence 3 [Teegarden & Weaver, 1994])
- The benefits of calcium supplement on the bone density of prepubertal girls remain unknown. (Grade of Recommendation D, Level of Evidence 3 [Teegarden & Weaver, 1994])

Vitamin D

Vitamin D Testing

- Blood 25(OH)D level is a good indicator of adequate vitamin D in the body. (Grade of Recommendation B, Level of Evidence 2+ [Hollis, 2005; Heaney et al., 2003])
- A blood 25(OH)D level of >30 ng/ml is considered physiologically adequate. (Grade of Recommendation B, Level of Evidence 2+ [Heaney, "Functional indices," 2004])
- Vitamin D level should be determined for osteoporosis patients or individuals with a high risk of vitamin D deficiency, and it can be tested after three months of supplement of ≥800 IU. (Grade of Recommendation C, Level of Evidence 2+ [Hollis, 2005; Heaney et al., 2003])
- Vitamin D [25(OH) D] insufficiency (<30 ng/ml) is a common disorder in many regions worldwide, including Asia. (Grade of Recommendation A, Level of Evidence 2+ [Mithal et al., 2009])

Vitamin D Supplement and Its Effect on the Prevention of Osteoporosis

- The recommended daily supplement of vitamin D is 800-1000 IU. (Grade of Recommendation B, Level of Evidence 2+ [Hollis, 2005; Heaney et al., 2003])
- Concomitant supplement of vitamin D and calcium is associated with increased bone density in postmenopausal women and men aged ≥50. (Grade of Recommendation A, Level of Evidence 2+ [Jackson et al., 2006] 1- [Boonen et al., 2007])
- Daily supplement of 800 IU vitamin D and 1000 mg calcium is associated with a lower incidence of hip and non-spinal fractures in the aged patient living in long-term care facilities. (Grade of Recommendation A, Level of Evidence 2+ [Bischoff-Ferrari et al., 2005] 1- [Tang et al., 2007])
- Daily supplement of vitamin D at 800 IU is associated with a lower incidence of falls in the aged patient. (Grade of Recommendation B, Level of Evidence 1- [Bischoff-Ferrari et al., "Higher 25-hydroxyvitamin D," 2004; Bischoff-Ferrari et al., "Effect of Vitamin D," 2004])
- Clinical trials of medications with proven efficacy for treating osteoporosis and bone fractures are all provided with sufficient supplement vitamin D and calcium. (Grade of Recommendation A, Level of Evidence 1++ [Hanley et al., 2010; Dawson-Hughes et al., 2010])

Bisphosphonates

- Reduction of the risk of spinal, non-spinal and hip fractures in postmenopausal women with osteoporosis can be achieved by the administration of bisphosphonates such as alendronate, risedronate and/or zoledronic acid. (Grade of Recommendation A, Level of Evidence 1++ [Wells et al., "Alendronate," 2010; Black et al., 1996; Cummings et al., 1998; Wells et al., "Risedronate," 2010; Harris et al., 1999; Reginster et al., 2000; McClung et al., 2001; Black et al., 2007])
- Reduction of the risk of spinal fractures in postmenopausal women with osteoporosis can be achieved by bisphosphonates such as ibandronate and/or etidronate. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2004; Wells et al., "Etidronate," 2010] 1+ [Eisman et al., 2008; Cramer et al., 2007])
- Osteoporosis-related hip fractures can be treated with zoledronic acid because its use is associated with lower incidence of bone fractures and lower mortality. (Grade of Recommendation A, Level of Evidence 1++ [Lyles et al., 2007])
- Reduction of bone fractures in men with osteoporosis can be achieved by the administration of bisphosphonates such as alendronate, risedronate and zoledronic acid. (Grade of Recommendation A , Level of Evidence 1++ [Zhong & Chen, 2009] 1+ [Sawka et al., 2005])
- For osteoporosis secondary to steroid use, bisphosphonates are effective in increasing bone density in the lumbar spine and femoral neck and minimizing bone loss, but evidence of its effect in the prevention of bone fractures is lacking. (Grade of Recommendation A, Level of Evidence 1++ [Homik et al., 2010])
- The effectiveness of bisphosphonates on secondary osteoporosis in children and adolescents is not established. (Grade of Recommendation A, Level of Evidence 1++ [Ward et al., 2010])
- The increased risk of esophageal or gastric cancer related to bisphosphonates has not been established. (Grade of Recommendation B, Level of Evidence 2++ [Cardwell et al., 2010)
- Long-term bisphosphonate use may lead to an increased risk of atypical femoral head fractures (including subtrochanteric fractures and femoral shaft fractures), which have a low absolute risk. More studies are required to confirm this relationship. (Grade of Recommendation B, Level of Evidence 2++ [Schilcher, Michaëlsson, & Aspenberg, 2011; Park-Wyllie et al., 2011])
- The relationship between bisphosphonate use and jaw bone necrosis in osteoporosis patients lacks supporting evidence, but attention as well as preventive measures should be exercised when high-dose injective bisphosphonates are used in cancer patients considering the risk of jaw necrosis. (Grade of Recommendation B, Level of Evidence 2++ [Khan et al., 2009; Silverman & Landesberg, 2009])
- Atrial fibrillation may be a complication of bisphosphonate use, but the evidence of their relationship is lacking. (Grade of Recommendation B, Level of Evidence 2++ [Loke, Jeevanantham, & Singh, 2009; Kim et al., 2010; Huang et al., 2010])
- Continuous bisphosphonate use is recommended for high fracture risk patients who have used it for at least 5 years. For patients with stable bone density, no fracture history and a low risk of bone fracture, cessation of bisphosphonates may be considered. (Grade of Recommendation A, Level of Evidence 1+ [Watts & Diab, 2010; Black et al., 2006])

Hormone, Tibolone, Selective Estrogen Receptor Modulators (SERMs)

- Hormone replacement therapy (HRT) is a preferred choice in the prevention of bone loss in postmenopausal women. (Grade of Recommendation A, Level of Evidence 1++ [Rossouw et al., 2002; Anderson et al., 2004; "Effects of hormone therapy," 1996])
- Conjugated equine estrogen (Premarin) at 0.625 mg daily (QD), 17β-estradiol at 1-2 mg or equivalent transdermal or transvaginal estrogen. Concomitant use with progesterone (e.g., medroxyprogesterone acetate [Provera] at 2.5-5 mg QD) is suggested. Estrogen alone should be provided to individuals who underwent hysterectomy. (Grade of Recommendation A, Level of Evidence 2++ [Prestwood et al., 2003; Ettinger et al., 2004] 1++ [Rossouw et al., 2002; Anderson et al., 2004; "Effects of hormone therapy," 1996])
- HRT is associated with a lower incidence of spinal compression or hip fractures in individuals aged ≤60. First-line therapies are not recommended for individuals aged ≥60 (Grade of Recommendation A, Level of Evidence 1++ [Cauley et al., 2003; Torgerson & Bell-Syer, 2001; Grady & Cummings, 2001; Delmas, 2002; Birkhäuser et al., 2008])
- HRT is contraindicated for postmenopausal women with risk factors of endometrial cancer, breast cancer and/or thrombosis. (Grade of Recommendation A, Level of Evidence 1++ [Cauley et al., 2003; Rossouw et al., 2002; Anderson et al., 2004; Utian et al., 2008])
- Tibolone is a tissue-selective estrogenic activity regulator (STEAR), where its selective tissue estrogenic or progestogenic activity comes from its metabolite. (Grade of Recommendation A, Level of Evidence 4 [Kloosterboer, 2001])
- Tibolone is associated with significant decrease of spinal and non-spinal fractures, along with lower risk of breast and colon cancer. (Grade of Recommendation A, Level of Evidence 2++ [Huber et al., 2002] 1++ [Gallagher et al., 2001; Studd et al., 1998; Cummings et al., 2008] 4 [Eden, 2005])
- Tibolone is associated with a significantly increased risk of stroke related to cardiovascular diseases. Postmenopausal women aged ≥60 should be aware of the risk of cardiovascular diseases and stroke episodes. (Grade of Recommendation A, Level of Evidence 1++ [Cummings et al., 2008])
- The incidence of bleeding, breast pain and headache is low in women using tibolone to control postmenopausal syndrome. (Grade of Recommendation B, Level of Evidence 2++ [Huber et al., 2002] 4 [Bianco et al., 2006])
- Raloxifene hydrochloride, a selective estrogen receptor modulator (SERM), acts differently from estrogen because it binds with estrogen receptors on the bone cells to achieve lower bone loss, improve bone density and effectively control the incidence of bone fractures without

the concern of breast and uterine side effects. The maximum daily dose is 60 mg. (Grade of Recommendation A, Level of Evidence 1++ [Delmas et al., 1997; Ettinger et al., 1999; Delmas et al., 2002; Cauley et al., 2001; Martino et al., 2004]
- National Health Insurance coverage is provided for raloxifene hydrochloride administered to postmenopausal women with osteoporosis-related spinal compression or hip fractures (and documentation in the medical records should be made). (Grade of Recommendation A, Level of Evidence 2++ ["Drug Coverage Plan," 2010])
- Raloxifene hydrochloride should not be used with bisphosphonates, calcitonin, active vitamin D3 and estrogen. (Grade of Recommendation A, Level of Evidence 2++ ["Drug Coverage Plan," 2010])

Parathyroid Hormone (PTH)

Taiwanese and Asian Studies

- Parathyroid hormone (PTH) is associated with increased lumbar spine BMD in Taiwanese women with severe osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Hwang et al., 2006])
- PTH is associated with increased lumbar and hip BMD in Asian women with severe osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Kung et al., 2006; Miyauchi et al., 2010])
- PTH is associated with increased bone formation markers in Taiwanese and Asian women with severe osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Hwang et al., 2006; Kung et al., 2006; Miyauchi et al., 2010])

Other Studies

- PTH is associated with increased lumbar spine and hip BMD in men and women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Neer et al., 2001; Orwoll et al., 2003; Kurland et al., 2000; Hodsman et al., 2005; Tashjian & Gagel, 2006] 1+ [Greenspan et al., 2007])
- PTH is associated with a significantly reduced risk of vertebral spinal and non-vertebral fractures in women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Neer et al., 2001; Hodsman et al., 2005; Tashjian & Gagel, 2006] 1+ [Greenspan et al., 2007])
- PTH is associated with increased bone formation markers in patients with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Neer et al., 2001; Orwoll et al., 2003; Kurland et al., 2000; Hodsman et al., 2005; Tashjian & Gagel, 2006; Greenspan et al., 2007])
- PTH is associated with pain relief and quality of life of osteoporosis-related bone fractures. (Grade of Recommendation A, Level of Evidence 1++ [Langdahl et al., 2009; Nevitt et al., 2006; Oglesby et al., 2003])
- PTH is associated with increased lumbar spine and hip BMD in steroid induced osteoporosis. (Grade of Recommendation A, Level of Evidence 1+ [Saag et al., 2007; Saag et al., 2009])
- No addition of effects was observed when PTH combined with other drugs for osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Black et al., 2003; Finkelstein et al., 2003])
- Other drugs for osteoporosis should be administered following PTH. (Grade of Recommendation A, Level of Evidence 1++ [Obermayer-Pietsch et al., 2008; Eastell et al., 2009; Black et al., 2005; Rittmaster et al., 2000])

Strontium Ranelate

Taiwanese and Asian Studies

- Strontium ranelate is associated with increased lumbar spine and hip BMD in Taiwanese and Asian women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Hwang et al., 2008; Liu et al., "Efficacy and safety," 2009])
- Strontium ranelate is associated with increased bone formation markers in Taiwanese women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Hwang et al., 2008])

Other Studies

- Strontium ranelate is associated with increased lumbar spine and hip BMD in men and women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Burlet & Reginster, 2006; Meunier et al., 2004; Reginster et al., 2005; Marie et al., 2001; Meunier et al., 2002] 1+ [Ringe, Dorst, & Farahmand, 2010])
- Strontium ranelate is associated with reduced risk of vertebral and hip femoral fractures in women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Burlet & Reginster, 2006; Meunier et al., 2004; Reginster et al., 2005])
- Strontium ranelate is associated with increased markers of bone formation and reduced bone resorption markers in women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Burlet & Reginster, 2006; Meunier et al., 2004; Reginster et al., 2005; Marie et al., 2001; Meunier et al., 2002])

Calcitonin

Other Studies

- Calcitonin is associated with improved bone density in postmenopausal individuals with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2008; Chesnut et al., 2000])
- Calcitonin is associated with a lower risk of vertebral fracture in postmenopausal individuals with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2008; Chesnut et al.; 2000])
- Calcitonin is associated with decreased bone turnover markers in postmenopausal individuals with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2000])
- Calcitonin directly acts on central nervous system to achieve analgesic effect, which can be used to relieve pain caused by osteoporosis-related fractures and improve quality of life after event. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2008; Clementi et al., 1984; Silverman & Azria, 2002; Chesnut et al., 2000; Lyritis et al., 1997; Lyritis et al., 1991; Knopp et al., 2005; Arinoviche et al., 1987; Lyritis et al., 1999])
- Calcitonin significantly improves the microstructure, volume and number of trabecular bone and minimizes the space between bone materials. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2008; Chesnut et al., 2005])
- Calcitonin is associated with improvement of lumbar BMD and pain relief. (Grade of Recommendation A, Level of Evidence 1++ [Chesnut et al., 2008; Trovas et al., 2002; Toth et al., 2005])
- Calcitonin is associated with improvement of lumbar and femoral BMD in individuals with steroid induced osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Cranney et al., 2000; Fraser & Adachi, 2009])

Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) Inhibitor

Other Studies

- RANKL inhibitor is associated with increased lumbar spine, hip and radial BMD in women with low bone density and osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Bone et al., 2008; Lewiecki et al., 2007; McClung et al., 2006; Cummings et al., 2009])
- RANKL inhibitor is associated with a significantly reduced risk of hip, vertebral spinal and non-vertebral fractures in women with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Cummings et al., 2009])
- RANKL inhibitor is associated with reduced bone turnover markers in patients with osteoporosis. (Grade of Recommendation A, Level of Evidence 1++ [Bone et al., 2008; Lewiecki et al., 2007; McClung et al., 2006; Cummings et al., 2009])
- RANKL inhibitor is associated with increased lumbar spine, hip and radial BMD in osteoporosis patients treated with bisphosphonates. (Grade of Recommendation A, Level of Evidence 1++ [Brown et al., "Comparison of the effect," 2009; Kendler et al., 2010])

Traditional Chinese Medicine

- "Kidney-nourishing" Chinese herbs are associated with lower serum estrone as well as increased estradiol level and BMD, suggesting its effectiveness in the prevention and treatment of osteoporosis. (Grade of Recommendation C, Level of Evidence 2- [Chi & Hui, 2000])
- Prescriptions for bone strengthening and kidney nourishment are associated with increased estrogen level, BMD and bone formation, especially in postmenopausal women with osteoporosis. (Grade of Recommendation C, Level of Evidence 2- [Pan, Li, & Yi, 2009])
- Concomitant use of the prescriptions for bone strengthening and kidney nourishment, prescriptions for blood and qi replenishment and vitamin D supplement is associated with significant differences in BMD, estradiol level, testosterone level and tartrate-resistant acid phosphatase after treatment. This is an effective approach for the prevention of osteoporosis as it inhibits bone resorption and promotes bone formation. (Grade of Recommendation C, Level of Evidence 3 [Shih & Gong, 2001])
- The combined Chinese-Western prescription based on six flavor rehmanni (liu wei di huang wan), a prescription for kidney nourishment, and anti-resorptives including nilestriol has been used for the treatment of primary osteoporosis in postmenopausal women and showed significant improvement of pain and BMD. (Grade of Recommendation C, Level of Evidence 3 [Chen, Niao, & Niao, 1999])
- The ingredients and their effects of the decoction of kidney- and spleen-nourishment and blood circulation-activating are: herba epimedii and fortune's drynaria rhizome for kidney warming, bone strengthening and nourishment of liver and kidneys. Chinese yam rhizome, the rhizome of *Atractylodes macrocephala* and the root of *Pilose asiabell* for spleen nourishment and qi replenishment. Chinese angelica root, rhizoma corydalis, red peony root, peony root peel and the rhizome of *Szechwan lovage* for enriching blood and promoting blood circulation, relaxing muscle/tendon/joints, removing meridian obstruction and blood stasis, and relieving pain. The rhizome of rehmannia, the root of rehmannia and the fruit of medicinal cornel as tonic for the liver and kidney and essence enrichment. These ingredients are combined to nourish the kidney and enrich vital essence; strengthen bone, muscle and ligaments; expel wind and dampness; activate blood circulation; dissipate blood stasis; promote qi circulation and relieve pain. Pharmacological studies showed that herba epimedii and fortune's drynaria rhizome possess sex hormone-like activities, while spleen-strengthening herbs are associated with enhancement of digestive function as well as better absorption and distribution of nutrients. Decoction of kidney- and spleen-strengthening and blood circulation-activating is

associated with improved BMD in postmenopausal women with osteoporosis and relieves back and bone pain. (Grade of Recommendation C, Level of Evidence 2- [Liu et al., "Efficacy of the treatment," 2009])

- Strong Bone capsule is a reasonable treatment for osteoporosis because it is effective against clinical symptoms in patients with osteoporosis, and it is associated with increased bone density. In terms of safety, no adverse cardiac, hepatic and/or renal reactions were observed in all subjects. Strong Bone capsule is safe and effective in the treatment of primary osteoporosis (kidney deficiency syndrome). (Grade of Recommendation C, Level of Evidence 2- [Li, Jhao, & Wun, 2005])
- The decoction of kidney- and spleen-invigoration and bone strengthening is safe, free of side effects, and is effective against the clinical symptoms of osteoporosis. (Grade of Recommendation C, Level of Evidence 3 [Jiao & Yang, 2009])
- Clinical studies showed that: flavones fortune's drynaria rhizome is associated with increased overall bone mass in elderly with osteoporosis, back pain relief, better bone strength at proximal femur and hip fracture prevention because of the promotion of collagen synthesis, bone turnover, bone formation, and the reduction of bone resorption. (Grade of Recommendation C, Level of Evidence 2- [Xi, 2008])
- Water extract of fortune's drynaria rhizome is expected to be provided to subjects with osteoporosis at clinical doses in clinical trials. Bone marker analysis, including bone density, blood alkaline phosphatase, and urine deoxypyridinoline and N-telopeptide of type I collagen (NTx) showed that the water extract of fortune's drynaria rhizome is associated with improvement of bone density and clinical symptoms. (Grade of Recommendation C, Level of Evidence 2- [Liu & Chen, 2003])

Definitions:

Level of Evidence

For the level of evidence, the authors adopted the recommendations by Scottish Intercollegiate Guidelines Network (SIGN) originally used by the National Health Research Institutes. It is classified into eight levels as follows:

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias.
2++	1. High quality systematic reviews of case control or cohort studies. 2. High quality case control or studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well conducted systematic reviews based on case control or cohort studies (with a low risk of confounding or bias and a moderate probability that the relationship is causal).
2-	Case control or cohort studies with a high risk of confounding or bias (and a significant risk that the relationship is not causal).
3	Non-analytic studies, e.g. case reports
4	Expert opinion

Grade of Recommendation

Grade of Recommendation	Properties
A	1. At least one meta-analysis, systematic review or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target patient. 2. Systematic reviews, RCTs, or most of the body of evidence consisting principally of studies rated as 1+, directly applicable to the target patient, and demonstrating overall consistency of results.
B	1. A body of evidence including studies rated as 2++, directly applicable to the target patient, and demonstrating overall consistency of results.

Grade of Recommendation	Properties
	2. Extrapolated evidence from studies rated as 1++ or 1+.
C	1. A body of evidence including studies rated as 2+, directly applicable to the target patient, and demonstrating overall consistency of results. 2. Extrapolated evidence from studies rated as 2++.
D	1. Evidence level 3 or 4. 2. Extrapolated evidence from studies rated as 2+.
It should be noted that recommendations of grade C or D are supported by evidence but their levels of evidence are not as strong as grade A or B. Therefore grade C or D should not be interpreted as negative measures in clinical settings.	

Clinical Algorithm(s)

An algorithm for procedures of post fall accidents is provided in the original guideline document.

Scope

Disease/Condition(s)

Osteoporosis and osteoporotic fractures

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Nursing

Nutrition

Obstetrics and Gynecology

Orthopedic Surgery

Pharmacology

Physical Medicine and Rehabilitation

Preventive Medicine

Radiology

Rheumatology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Chiropractors

Hospitals

Nurses

Occupational Therapists

Physical Therapists

Physician Assistants

Physicians

Guideline Objective(s)

- To provide guidance for clinicians on the prevention, diagnosis and treatment of osteoporosis
- To provide practical recommendations and approaches based on the systematic review of published literature or guidelines from developed countries and academic groups for practitioners in Taiwan

Target Population

Adults at risk for or diagnosed with osteoporosis

Interventions and Practices Considered

Diagnosis/Evaluation

1. Physical examination, including Osteoporosis Self-assessment Tool for Asians (OSTA)
2. Bone turnover markers
3. Quantitative ultrasound (QUS)
4. Bone density testing, using dual energy x-ray absorptiometry (DXA)
5. T-score
6. History of fracture
7. Risk assessment
    - One-Minute Osteoporosis Risk Awareness test
    - Evaluation of clinical factors
    - Fracture risk assessment tool (FRAX)

Prevention/Treatment

Non-pharmaceutical

1. Dietary considerations, including calcium and dairy products, vitamin D, phosphorus, protein, vitamin K, vegetarian diet, and use of table salt/sodium
2. Exercise and activity, including weight-bearing activities, resistive exercises, weight training
3. Lifestyle considerations, including body mass index, smoking status, and alcohol intake
4. Fall prevention interventions
    - Fall assessment tool
    - Hip protectors
    - Review of medications
    - Multiple strategies approach
    - Environmental considerations (lighting, access, clothing and footwear)
5. Surgical management
    - Early surgical intervention (hip arthroplasty, vertebroplasty)
    - Assistive devices

Pharmaceutical

1. Calcium supplements
2. Vitamin D supplements
3. Bisphosphonates
4. Hormone replacement therapy, including tibolone and selective estrogen receptor modulators (SERMs)
5. Parathyroid hormone (PTH)
6. Strontium ranelate
7. Calcitonin
8. Receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor
9. Traditional Chinese medicine

Major Outcomes Considered

- Bone mineral density
- Fracture rates
- Loss of function
- Mortality and morbidity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

In the preparatory meeting for the "Consensus on the Treatment and Management of Osteoporosis" held on January 19, 2010, it was determined that the contents of this guideline would be arranged in five topics: definition and pathophysiology, epidemiology, diagnosis and follow-up, approaches for prevention and treatment without medication, and with medication.

In each topic, the search included most recent and well recognized clinical guidelines worldwide (for example, the one by International Osteoporosis Foundation), and the clinical study literature in English and Chinese between 2005 and 2010 by Medline search. The exclusion

criteria included animal experiments, description of clinical techniques (technical note and operative nuance), and literature written in languages other than English and Chinese. The keywords and strategies were decided by each editor of each chapter and are listed in the original guideline document.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

For the level of evidence, the authors adopted the recommendations by Scottish Intercollegiate Guidelines Network (SIGN) originally used by the National Health Research Institutes. It is classified into eight levels as follows:

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias.
2++	1. High quality systematic reviews of case control or cohort studies. 2. High quality case control or studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well conducted systematic reviews based on case control or cohort studies (with a low risk of confounding or bias and a moderate probability that the relationship is causal).
2-	Case control or cohort studies with a high risk of confounding or bias (and a significant risk that the relationship is not causal).
3	Non-analytic studies, e.g. case reports
4	Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Critical appraisal of evidence from literature

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, opinions from experts were used.

Rating Scheme for the Strength of the Recommendations

Grade of Recommendation	Properties
A	1. At least one meta-analysis, systematic review or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target patient. 2. Systematic reviews, RCTs, or most of the body of evidence consisting principally of studies rated as 1+, directly applicable to the target patient, and demonstrating overall consistency of results.
B	1. A body of evidence including studies rated as 2++, directly applicable to the target patient, and demonstrating overall consistency of results. 2. Extrapolated evidence from studies rated as 1++ or 1+.
C	1. A body of evidence including studies rated as 2+, directly applicable to the target patient, and demonstrating overall consistency of results. 2. Extrapolated evidence from studies rated as 2++.
D	1. Evidence level 3 or 4. 2. Extrapolated evidence from studies rated as 2+.
It should be noted that recommendations of grade C or D are supported by evidence but their levels of evidence are not as strong as grade A or B. Therefore grade C or D should not be interpreted as negative measures in clinical settings.	

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The initial draft of this guideline was reviewed by a multidisciplinary peer panel after its completion on July 31, 2010. On October 10, 2010, recommendations were provided by oral comments and in writing, which included format consistency, fluency of translated texts, a pool of reference based on the most recent literature and the addition/removal of chapters and sections. The final draft was approved by the panel on November 10, 2010, and the review by experts who had not participated in the creation of this guideline was coordinated by the National Health Research Institutes.

Evidence Supporting the Recommendations

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with osteoporosis

Potential Harms

- Calcium supplement (1000 mg) and vitamin D (400 IU/day) for healthy postmenopausal women provide little effect, and these may cause a higher risk of renal stones.
- Tibolone is associated with a significantly increased risk of stroke related to cardiovascular diseases. Postmenopausal women aged ≥60 should be aware of the risk of cardiovascular diseases and stroke episodes.
- Bisphosphonates
  - Esophageal cancer: Oral bisphosphonates may induce gastrointestinal discomfort (e.g., acid reflux, nausea and vomiting, esophagitis or esophageal ulcer), but the evidence regarding the relationship between bisphosphonates and the risk of esophageal or gastric cancer is inadequate.
  - Atypical femoral head fractures including subtrochanteric fractures or diaphyseal fractures: Long-term bisphosphonate use may lead to an increased risk of these fractures, which have a low absolute risk. More studies are required to confirm this relationship.
  - Osteonecrosis of the jaw: Cases of jaw bone necrosis have been reported since 2003, while the relationship between osteonecrosis and bisphosphonate use awaits further exploration. Attention should be exercised on the risks when high-dose injective bisphosphonates are administered to cancer patients. As the relationship between cessation of bisphosphonates and lower risk of jaw bone necrosis has not been established, these medications should be used with care.
  - Atrial fibrillation: In a clinical trial of zoledronic acid (HORIZON Pivotal Fracture Trial), a few cases of atrial fibrillation were

reported, but similar risk was not observed in other clinical trials. No evidence was identified in the long-term monitoring report from the U.S. Food and Drug Administration (FDA), registered studies of marketed drugs and Taiwanese studies showing the association of bisphosphonate with an increased risk of atrial fibrillation.

- Parathyroid hormone: Adverse reactions include hypercalcemia, hypercalciuria, nausea, headache, leg cramps and orthostatic hypotension, and usually temporary and mild. Teriparatide is not recommended for patients with history of metastatic bone tumors or bone malignancy because its long-term use at high doses has been associated with a higher risk of osteosarcoma in the animal model. It is not recommended to be used on patients with Paget's disease or metabolic bone diseases.
- Strontium ranelate: The side effect is similar to those of placebo. Most are temporary mild adverse reactions, including diarrhea, nausea, headache and dermatitis, which may occur at the start of treatment. Precaution is advised in patients with phenylketonuria (PKU) and venous thromboembolism (VTE). Cessation is recommended for patients experiencing drug rash with eosinophilia.
- Receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor: In clinical trials comparing denosumab with placebo, side effects identified include infection, constipation, sore throat, rash and diverticulitis that are usually mild.
- Side effects of hormone therapy include breast pain, temporary nausea, mild edema, and abnormal vaginal spotting. The result of the double blinded study in the large Women's Health Initiative (WHI) showed that more than 5 years of hormone therapy may increase the risk of breast cancer, and elderly postmenopausal women (>65 y/o) may also be associated with a higher risk of coronary heart disease.
- The incidence of bleeding, breast pain and headache related to estrogen and progesterone is lower in individuals treated with tibolone because it does not have estrogenic activity on the endometrium and breast. Other side effects including dizziness, pruritus, mild nausea and slight weight gain may be more significant.
- Raloxifene is associated with a higher risk of hot flushes and leg cramps when compared to the control group in some studies. Considered a severe side effect, increased incidence of venous thromboembolism (VTE) was noted in raloxifene users (3.5/1,000) in the first two years when compared to the control group (1.7/1,000). This difference became insignificant in the long term.
- Since its introduction, more than 20 years of clinical experience has shown that Miacalcic has an excellent safety profile. Side effects are usually mild and are associated with dose level and first use. Temporary flush, nausea and vomiting may occur at the start of treatment with injective, and these side effects can be minimized by switching to subcutaneous doses, using at a lower dose, or using nasal spray at night. Nasal spray may be associated with local side effects such as nasal discomfort, nasal congestion and sneezing. To avoid the risk of allergic reactions to polypeptides, the main component of salmon calcitonin, skin test is suggested for patients with suspected hypersensitivity.

Contraindications

Contraindications

- Hormone replacement therapy (HRT) is contraindicated for postmenopausal women with risk factors of endometrial cancer, breast cancer and/or thrombosis.
- Raloxifene hydrochloride should not be used with bisphosphonates, calcitonin, active vitamin D3 and estrogen.

Qualifying Statements

Qualifying Statements

- The goal of this guideline is to provide guidance for clinicians on the prevention, diagnosis and treatment of osteoporosis. Clinicians are strongly encouraged to select the best strategy tailored to the condition of each patient.
- The application of this guideline is to provide guidance on treatment plans for clinicians, meaning that this guideline does not suggest a standard of care, nor does it discourage approaches that are not included. In this guideline, financial cost is not the main topic because the policies of National Health Insurance and the related coverage are not emphasized. This guideline cannot be used as a substitute for clinicians' experience, and proper judgements should be made by clinicians based on the clinical particulars of each patient and other objective factors to select the best treatment.
- The information in this guideline is designed to aid clinicians and patients in making decisions about appropriate care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Bureau of Health Promotion, Department of Health, Taiwan, National Health Research Institutes, Taiwanese Osteoporosis Association. Taiwan osteoporosis practice guidelines. Taiwan (ROC): Bureau of Health Promotion, Department of Health, Taiwan; 2011 Dec. 110 p. [261 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Developer(s)

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National Health Research Institutes (Taiwan) - Nonprofit Research Organization

Taiwanese Osteoporosis Association - Disease Specific Society

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Guideline Committee

Not stated

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Financial Disclosures/Conflicts of Interest

This guideline is created based on the consensus of local experts and evidence from medical research, and there is no conflict of interest and financial interest in individuals or groups.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Bureau of Health Promotion, Department of Health, Taiwan (BHP DoH) Web site .
Also available in Chinese from the BHP DoH Web site .

Availability of Companion Documents

None available

Patient Resources

Patient education materials are available in Chinese from the Taiwanese Osteoporosis Association Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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